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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/173,864	10/16/1998	ROBERT D. IVARIE	24011-0002	4740

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WILLIAM SCHMONSEES
HELLER, EHRMAN, WHITE & MCAULIFFE LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER
KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	09/173,864	IVARIE ET AL.	
	Examiner	Art Unit	
	S. Kaushal	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,27,35,43-45,53-55 and 57-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19,27,35,43-45,53-55 and 57-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's response filed on 01/01/01 has been acknowledged.

Claims 21, 25, 29, 33-34, 41-42, 46, 48-49, 52 and 56 were canceled.
Claims 58 and 59 were newly filed.
Claims 19, 27, 35, 43-45, 53-55 and 57 were amended.
Claims 19, 27, 35, 43-45, 53-55 and 57-59 were pending and were examined in this office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

► *If the claims are amended, added and/or canceled in response to this office action the applicants are required to follow Amendment Practice under 37 CFR § 1.121 (http://www.uspto.gov) and* <u>*A CLEAN COPY OF **ALL** PENDING CLAIMS IS REQUESTED.*</u>

Applicant's arguments filed 01/10/02 have been fully considered but they are not persuasive, for the reasons of record as set forth in the earlier office action (Paper No.18, 04/25/01).

Claim Rejections - 35 USC § 112

Claims 19, 27, 35, 43-45, 53-55 and 57-59 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic chicken encoding in their germ lines a human Interferon (huIFN) transgene, which results in the production of the huIFN contained in the egg whites of transgenic eggs, does not reasonably provide enablement for a transgenic chicken encoding in their germ lines Erythropoietin and GM-CSF transgenes, which results in the production of the transgene contained in the egg whites of transgenic eggs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention **commensurate in scope** with these claims. for the same reasons of record as set forth in the official action mailed on Paper No 18, 04/25/01.

The applicant argues that invention as claimed after recent amendment is limited to a particular bird "chicken". The applicant further argues that the specification teaches the production of exogenous protein in tubular gland cells of the oviduct because it is in those cells that synthesis egg white protein are produced and deposited in the egg white (response, page 5, ¶ 3). The applicant further argues that the exogenous proteins produced by the present invention are **Interferon, Erythropoietin and GM-CSF** driven by a constitutive promoter (response, page 5, ¶ 4). The applicant further argues that the present specification as confirmed by the declaration of Dr. Rapp teach the production of fully transgenic chickens (i.e. G2 offspring) by breeding chimeric founders. Applicant have provided data showing that the G1 and G2 progeny produce Interferon, Erythropoietin and GM-CSF in their serum as well as egg white of eggs laid

by transgenic hens (response, page 6, ¶ 2-3). The applicant concluded that invention as claimed does not require undue amount of experimentation in view of applicant's disclosure

Dr. Jeffrey Rapp's declaration *(attached to Paper No. 16, 02/21/01)* under 37CFR 1.32 states that the out of 1597 offsprings one rooster was found transgenic "Alphie" whose G2 offsprings hens produces an average of 900nanograms/ml hu-**Interferon** in the egg white material (declaration, page 7, para 7).

However, this not found fully persuasive because the full scope of the invention as claimed is not supported by Dr. Jeffrey Rapp's declaration as submitted. The scope of instant invention encompasses a transgenic chicken and a transgenic egg thereof, which contain an exogenous gene product selected from Interferon, Erythropoietin and GM-CSF. The declaration fails to disclose transgenic chickens encoding in their germ lines **Erythropoietin and GM-CSF** transgenes, which results in the production of the transgene contained in the egg whites of transgenic eggs. At best Dr. Jeffrey Rapp's declaration only teaches a transgenic rooster "Alphie" whose G2 offsprings hens produces an average of 900 nanograms/ml hu-**Interferon** in the egg white material. However, it is unclear from Dr. Jeffrey Rapp's declaration **what is the type of hIFN produced** by the progeny of transgenic chicken "Alphie". The general knowledge in the Interferon art is such that there are various types of human Interferon(s), which are structurally and functionally distinct (e.g. hIFNα, hIFNγ). Therefore Dr. Jeffrey Rapp's declaration fails to disclose all aspects of invention as claimed which encompass a transgenic chicken and a transgenic egg thereof which contain an exogenous gene product selected from Interferon (any types), Erythropoietin and GM-CSF.

As stated in the earlier office action, the art at the time of filing clearly states that the making of transgenic birds is highly unpredictable because the complexities of egg formation make the earliest stages of chick-embryo development relatively in-accessible (Sang TIBTECH 12:415-420, 1994, page 415, col.2 para.2, *ref. of record*). Furthermore, the making of chimeric birds is technically demanding as its require the development of methods that enhances the survival of embryonic cells and an increase in frequency of chromosomal integration of injected DNA (Sang, page 416, col.1 para.3). Furthermore, ex-vivo transfection of blastodermal cells and reimplantation into an egg has not show to transmit the transgene through germ lines. In addition, the development of chicken embryonic stem cells that can be grown for longer periods in culture to allow the targeted recombination events is highly unpredictable (Sang page 417, col.1 para. 1-2). Furthermore, it is unclear how a particular transgene would effect the development of mature birds and the production of transgenic eggs. Therefore, considering the unpredictable nature of avian transgenic art, the declaration and the specification as filed fails to support the full scope of invention as claimed. Since to make and test is not the standard for enablement, one skill in the art would have to engage in excessive and undue amount of experimentation.

Furthermore, replication defective retroviral vector has been used to obtain germ line transmission of transgenes resulting in a wide variety of tissues, however tissue-specific expression has not been achieved (Simkiss, Transgenic birds, animals with novel genes, Mclean ed, Cambridge Univ.Press NY pages 106-137, 1994, see paragraph bridging pages 118-119, *ref. of record*). The specification fails to show the expression of any exogenous protein in the tubular gland cells of oviduct or magnum tissue of any chicken. The specification only provided a

prophetic example in fig-6, which illustrates magnum-specific gene expression in magnum and non-magnum cells (page 13, line 9-13). In addition, it is general knowledge in the art the retroviral viral vectors integrate into the host genome by random insertion. This is even clear from Dr. Jeffrey Rapp's declaration who teaches that "Alphie" was one unexpected finding among 1597 offsprings of three G0-rosters obtained from approximately 300 chimeric chickens (declaration page para 6 and7). In addition applicant fails to disclose transgenic chickens encoding in their germ lines Erythropoietin or GM-CSF transgenes, which results in the production of the transgene contained in the egg whites of transgenic eggs. Further suggesting that making a transgenic chicken is highly unpredictable especially when a retrovirus is used to deliver the transgene of interest to make chimeric chickens.

Applicant's argument alone cannot take place of evidence lacking in the record. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). *In instant case making any transgenic chickens to produce an exogenous gene product of interest, wherein the transgene product is contained in the transgenic egg is not considered routine and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.* See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991).

Thus, in view of lack of specific guidance in the specification and the declaration, and considering the state of the art, the skilled artesian at the time of filing would be unable to use the claimed invention, without an excessive and undue amount of experimentation. The quantity of

experimentation required would include making transgenic chickens encoding any type of human Interferon, Erythropoietin and GM-CSF transgenes, wherein the transgenic chicken express the transgene product in its egg white.

Claim Rejections - 35 USC § 102

Claim 57 is rejected under 35 U.S.C. 102(b) as being anticipated by Sekellick (WO 95/11302, 1995, *reference of record*). The cited art teaches chicken **Interferon** gene and a method of producing biologically active recombinant interferon (see pages 22-25). The scope of instant claims encompasses a product by process, wherein the product is indistinguishable from the product cited in the prior art of record. In instant case the isolated Interferon (as claimed) is indistinguishable from the purified Interferon preparation as taught by Sekellick. Thus the invention as claimed is clearly anticipated by the cited prior art of record.

Claim 58 is rejected under 35 U.S.C. 102(b) as being anticipated by Davis et al (Biochem 26(9):2633-8, 1987, see abstract). The cited art teaches purified recombinant human **Erythropoietin** protein. The scope of instant claims encompasses a product by process, wherein the product is indistinguishable from the product cited in the prior art of record. In instant case the isolated Erythropoietin (as claimed) is indistinguishable from the purified Erythropoietin preparation as taught by Davis et al. Thus the invention as claimed is clearly anticipated by the cited prior art of record.

Claim 59 is rejected under 35 U.S.C. 102(b) as being anticipated by Nakayama et al (EP 281069, 1998, see abstract). The cited art teaches purified recombinant human **GM-CSF** protein. The scope of instant claims encompasses a product by process, wherein the product is indistinguishable from the product cited in the prior art of record. In instant case the isolated GM-CSF (as claimed) is indistinguishable from the purified GM-CSF preparation as taught by Nakayama. Thus the invention as claimed is clearly anticipated by the cited prior art of record.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Irem.Yucel can be reached on (703) 305-1998. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Zeta Adams, whose telephone number is (703) 305-3291.

S.Kaushal
Patent examiner

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER